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Neuron-Glia Interactions: May 24S-Hydroxycholesterol Be a Signal Molecule in the Retina in the Course of Retinal Ganglion Cell Loss?

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Abstract

Purpose:Cholesterol 24S-hydroxylase (CYP46A1) is an enzyme which converts cholesterol into 24S-hydroxycholesterol (24SOH). CYP46A1 is expressed in retinal ganglion cells (RGC) and in activated glia. Glial cells are known to maintain an intimate relationship with neurons, especially in the course of neurodegeneration. Activated glia may affect the survival of RGC but may also be protective against neuronal loss in response to damage. The purpose of our study was to emphasize the role of CYP46A1 and 24SOH in these neuron-glia interactions within the context of RGC loss.

Methods:Sprague-Dawley rats were submitted to elevation of intra-ocular pressure (IOP) by argon-laser photocoagulation of limbus, episcleral veins and trabeculum in one eye. IOP was regularly monitored by tonometry and the rats were euthanized at day 3, 14, 30 and 60 (n=10 at each time point). 24SOH was measured in plasma and retina by isotope dilution gas chromatography-mass spectrometry using internal deuterated standard. Immunostaining and flow cytometry were carried out to analyze the expression of CYP46A1, GFAP and vimentin as markers for glial activation, and Thy1.1 as a marker for RGC.

Results:Sustained high IOP (36.04±9.37mmHg at day 3) was observed in experimental eyes from day 1 to day 21. IOP returned to baseline (8.80±1.99mmHg) afterwards. Glial activation was observed at early times as illustrated by the increased expression of GFAP and vimentin. Glial activation was observed bilaterally at these time points. Meanwhile, we observed a loss of RGC. CYP46A1 expression remained relatively constant until day 30 and declined thereafter in experimental eyes. Data on the quantification of 24SOH in the retina consistently support this finding.

Conclusions:Activation of glia in the retina was found to counterbalance the loss of RGC in response to elevation of IOP. Induction of CYP46A1 by glial cells and production of 24SOH may participate to this neuron-glia talk.

Keywords: lipids • retinal glia • ganglion cells